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Inside This Issue

STATE-OF-THE-ART PAPER

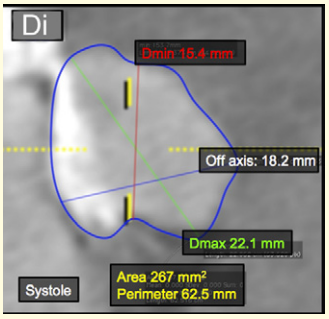
The National Heart, Lung, and Blood Institute (NHLBI) recently sponsored a workshop entitled "Cardiac Transplantation Research in the Next Decade: A Goal to Evidence Based Outcomes." The participants identified the most urgent knowledge gaps regarding heart transplantation and divided them into 4 specific research directions: 1) enhanced phenotypic characterization of the pre-transplant population; 2) donor–recipient optimization strategies; 3) individualized immunosuppression therapy; and 4) investigations of immune and nonimmune factors affecting late cardiac allograft outcomes. The participants strongly urged concerted efforts to enroll every transplant recipient into a clinical study and to increase collaborative networks given the small number of transplants that occur every year.

EDITORIALS AND VIEWPOINTS

The federal government has investigated several institutions for implantable cardioverter-defibrillator (ICD) procedures that may have been in violation of the criteria set forth in a National Coverage Determination. Steinberg and Mittal describe their experience and responses to such an audit. They identified 7 categories of patients flagged as inappropriate: 1) those that truly were inappropriate; 2) secondary prevention patients where the index event was not properly recognized because it occurred at outside facility; 3) patients with cardiomyopathy presenting with syncope; 4) trivial cardiac enzyme elevation coded as acute MI; 5) ICD implantation when the acute device need was bradycardia; 6) PCI not anticipated to improve chronic LV dysfunction within 90 days; and 7) ICD implantation near the end of the 90 day post-revascularization period. A careful audit found that only 15% of the cases flagged as inappropriate failed to have an acceptable explanation rendering them appropriate. The authors conclude with a description of the procedures they have implemented to reduce the risk of future audits while still ensuring optimal patient care.

(continued on page A-18)

CLINICAL RESEARCH



IMAGING IN TRANSCATHETER AORTIC VALVE REPLACEMENT

CT Imaging Improves Accuracy of Aortic Annular Sizing for TAVR **1275**

Hasan Jilaihawi, Mohammad Kashif, Gregory Fontana, Azusa Furugen, Takahiro Shiota, Gerald Friede, Rakhee Makhija, Niraj Doctor, Martin B. Leon, Raj R. Makkar

Recent studies have shown clear discrepancies between echocardiographic and computed tomographic (CT) aortic annular measurements for sizing in patients undergoing transcatheter aortic valve replacement (TAVR). Jilaihawi and colleagues sought to determine if these differences were clinically relevant. Cross-sectional CT measurements were slightly more predictive for post-TAVR paravalvular regurgitation then circumference-derived measurements, while traditional echocardiographic measures were not predictive. These data support using cross-sectional CT measures as the gold standard for aortic annular sizing prior to TAVR.

IMAGING IN TRANSCATHETER AORTIC VALVE REPLACEMENT

Imaging in TAVR Aortic Annular Assessment by MDCT Predicts Moderate or Severe Paravalvular Regurgitation After TAVR **1287**

Alexander B. Willson, John G. Webb, Troy M. LaBounty, Stephan Achenbach, Robert Moss, Miriam Wheeler, Christopher Thompson, James K. Min, Ronen Gurvitch, Bjarne L. Norgaard, Cameron J. Hague, Stefan Toggweiler, Ronald Binder, Melanie Freeman, Rohan Poulter, Steen Poulsen, David A. Wood, Jonathon Leipsic

Willson and colleagues performed a multicenter, retrospective analysis of over 100 patients who underwent multidetector computed tomography (MDCT) prior to transcatheter aortic valve replacement (TAVR) to determine if MDCT-derived aortic annular dimensions could predict which patients would develop para-aortic regurgitation (PAR) after the procedure. Moderate or severe PAR was associated with tissue heart valve (THV) undersizing compared to MDCT measurements, while annular eccentricity was not. MDCT-derived annular measurements, particularly the mean diameter and the cross-sectional area, are predictive of moderate or severe PAR following TAVR.

(*continued on page A-19*)

HEART RHYTHM DISORDERS

Patients With Metabolic Syndrome at Increased Risk for Arrhythmia Recurrence After AF Ablation 1295

Sanghamitra Mohanty, Prasant Mohanty, Luigi Di Biase, Bai Rong, Agnes Pump, Pasquale Santangeli, David Burkhardt, Joseph G. Gallinghouse, Rodney Horton, Javier E. Sanchez, Shane Bailey, Jason Zagrodzky, Andrea Natale

Metabolic syndrome (MS), a pro-inflammatory state with hypertension, diabetes, dyslipidemia, and obesity, appears to pre-dispose patients to atrial fibrillation (AF). Mohanty and colleagues investigated whether or not MS affects the outcomes of catheter ablation of AF. In 1,500 consecutive AF ablation patients, subjects with MS were more likely to have arrhythmia recurrence during 2 years of follow-up. This was driven mostly by higher recurrence rates in those with permanent AF. These results help to clarify the relationship between MS and AF and will help to counsel patients on the likelihood of success of AF ablation procedures.

Editorial Comment: Samuel J. Asirvatham, Zhen Jiao, p. 1302

CARDIAC PHARMACOLOGY

Differences in the Pharmacokinetic and Pharmacodynamic Effects of PPIs on Clopidogrel 1304

Andrew L. Frelinger III, Ronald D. Lee, Darcy J. Mulford, Jingtao Wu, Sai Nudurupati, Anu Nigam, Julie K. Brooks, Deepak L. Bhatt, Alan D. Michelson

The metabolism of clopidogrel into it active metabolite requires cytochrome P450s, including CYP2C19. Felinger and colleagues studied whether various proton pump inhibitors (PPIs) affect the pharmacokinetics and pharmacodynamics of clopidogrel by studying subjects who were homozygous for CYP2C19 extensive metabolizer genotype. The area under the curve for clopidogrel active metabolite ($clopidogrel_{AM}$) decreased significantly with omeprazole and esomeprazole but not with dexlansoprazole or lansoprazole. Results were similar for the effect on VASP platelet reactivity index. These results suggest that the potential of PPIs to attenuate clopidogrel efficacy could be minimized by using dexlansoprazole or lansoprazole rather than esomeprazole or omeprazole in patients who require both.

(continued on page A-20)

VALVULAR HEART DISEASE

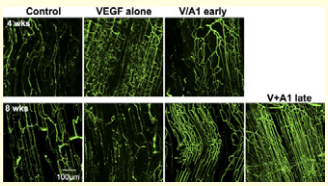
Similar Efficacy With MitraClip Therapy in Patients With and Without AF **1312**

Howard C. Herrmann, Zachary M. Gertz, Frank E. Silvestry, Susan E. Wiegers, Y. Joseph Woo, James Hermiller, Douglas Segar, David Heimansohn, William Gray, Shunichi Homma, Michael Argenziano, Andrew Wang, James Jollis, Mark B. Lampert, John Alexander, Laura Mauri, Elyse Foster, Donald Glower, Ted Feldman

The EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) compared the MitraClip (Abbott Vascular, Abbott Park, Illinois) procedure to surgical repair for patients with mitral regurgitation (MR). Hermann and colleagues performed a substudy to explore the impact of atrial fibrillation (AF) in their patients, whether treated with the MitraClip or surgically. Pre-existing AF was found in patients who were older, had more advanced disease, and were more likely to have functional MR. There were similar technical and clinical outcomes to 12 months in patients with and without AF treated with the MitraClip. There was no interaction between rhythm and MR reduction with either treatment modality at 12 months. AF is associated with more advanced valvular disease and noncardiac comorbidities, but does not seem to affect the therapeutic benefits of MitraClip therapy.

PRE-CLINICAL RESEARCH

Improved Results With Temporally Separated VEGF and Ang-1 Gene Transfer **1320**



Alexandra H. Smith, Michael A. Kuliszewski, Christine Liao, Dmitriy Rudenko, Duncan J. Stewart, Howard Leong-Poi

Single gene delivery of vascular endothelial growth factor (VEGF) results in immature neovessels that ultimately regress. Smith and colleagues notes that angiopoietin (Ang)-1 acts later to induce vessel maturation and, therefore, studied giving Ang-1 4 weeks after VEGF transfection. Unilateral hindlimb ischemia was induced in rats who then underwent ultrasound-mediated gene delivery of plasmid deoxyribonucleic acid. Compared to VEGF alone and VEGF/Ang-1 simultaneously, temporally separated VEGF and Ang-1 delivery, resulted in improved blood flow, vessel density and flow reserve at 8 weeks. These results confirm that delivering Ang-1 after VEGF has induced neovascularization leads to more sustained and functional improvements.